REMARKS

Claims 30 to 36 have been submitted to more particularly define Applicants' invention and are active in this application. Reconsideration is respectfully requested. It is respectfully submitted that the foregoing amendments substantially advance the prosecution of this application and place it is condition for allowance. The subject invention is predicated on the discovery by Applicants that patients with Alzheimer's disease have a form of butyrylcholinesterase that possesses an altered glycosylation pattern when compared to the form of butyrylcholinesterase typically found in patients not afflicted with Alzheimer's disease. Accordingly, butyrylcholinesterase with an altered glycosylation pattern acts as a biomarker for the detection of Alzheimer's disease. The subject method is reflected in Claims 30 to 36 submitted above.

Turning to the Office Action, the points raised therein will be addressed in the context of Claims 30-36. As required, Applicants have inserted by amendment of the specification the priority information concerning parent application Serial No. 09/829,446. Applicants would note, however, that when the present application was filed as a continuation, the box requesting this information be inserted into the specification was checked, hence it should have already been in the specification.

The rejections to Claims 20-25 as not being of proper dependent form are obviated by the cancellation thereof and, it is believed, would not apply to the present claims. The rejections of Claims 20-23 under the first paragraph of 35 U.S.C. §112 as failing to comply with the written description requirement thereof and containing new matter are obviated by the cancellation thereof and, it is respectfully submitted, would not apply to Claims 30-34. In the Office Action under reply, the Examiner states that the present specification provides for a range in Table 1 and such a range does not

support numerical limits, such as "at least about 8%" because it has an upper limit. Applicants respectfully disagree.

The diagnostic determination of the subject invention is a screening test and, as such, is predicated on a threshold determination. Once that threshold has been crossed and there is a positive indication that the patient may in fact be afflicted with Alzheimer's disease, the upper range of the determination is immaterial. Applicants have taught in their specification in Table 1 the average percentage of butyrylcholinesterase unbound to concanavalin A (Con A), which is indicative of butyrylcholinesterase having an altered glycosylation pattern, and the level of unbound butyrylcholinesterase that is indicative of the presence of Alzheimer's disease, given that there will be considerable variation among individual patients as would be readily apparent to those skilled in the medical arts. Therefore, it is respectfully submitted that the rejection would not apply to Claims 30-36.

It is respectfully submitted that the rejection of Claims 19-29 under the first paragraph of 35 U.S.C. §112 as failing to comply with the written description requirement in that Applicants' specification would not reasonably convey to one of ordinary skill in the art that Applicants' were in possession of the claimed invention at the time the application was filed would not apply to Claims 30-36. The rejection would appear to have been predicated on the assumption that Applicants have not adequately qualified the relation between the amount of butyrylcholinesterase ("BChE") unbound to Con A and that unbound to Lens Culinaris (LCA), i.e. that it is necessary to determine the presence of both in order to diagnose Alzheimer's disease ("AD"). In point of fact, this is not correct.

As is evident from Table 1 in Applicants' specification, BChE with an altered glycosylation pattern as a biomarker for AD displays differential bindings to both Con A

and LCA lectins, i.e. differential binding as opposed to normal BChE. However, as is also evident from Table 1, while the presence of a different binding pattern to Con A is specific to the BChE that is a biomarker for AD, the differential binding pattern to LCA is not specific, note columns 4 and 5 of the LCA binding which indicate that the increased binding of BChE to LCA may be indicative of AD or non-AD type dementia (DNAT) or other neurological disorders (ONO). Presumable, while not wishing to be bound by a particular theory, a patient afflicted with ONO or DNAT may also have a form of BChE that demonstrates reduced binding of LCA. It follows, therefore, the LCA lectins cannot be utilized as a diagnostic screen for AD as binding for it is not specific to AD. Hence, because binding to Con A is a specific indicator of AD, it is evident that Applicants have meet the requirement for written description of the invention in their specification as discussed above.

Applicants agree with the discussion in the Office Action under reply that the specification teaches only a single pattern of altered lectin binding by BChE as an indication of the presence of AD. However, Applicants respectfully disagree with the statements concerning the need for the present specification to contain a teaching of the actual structure of the glycosylation on the BChE that is unbound to Con A, or that there should be disclosure of other chemical means of determining glycosylation. Applicants' determination is a screening test based on threshold amounts of BChE unbound to Con A. While there is BChE unbound to LCA as well, that is not specific to Alzheimer's disease as discussed above. Hence, further definition of the affinity considerations as set out in the Office Action under reply are not necessary in order for the specification to enable Claims 30-36.

It is respectfully submitted that the rejections of Claims 19-29 as being indefinite under the second paragraph of 35 U.S.C. §112 would not apply to Claims 30-36. In regard to the use of the term "affinity" Applicants submit that it would be apparent to

one of ordinary skill in the art that, in the context of the present invention, the term is synonymous with the usage in affinity chromatography in the general sense that the scientific community does not place undue scientific meaning thereon. However, the term is not present in Claims 30-36, thus rendering the objection moot. The claims recite specifically the determination of the amount of BChE unbound to Con A and compare it against the total BChE in the sample.

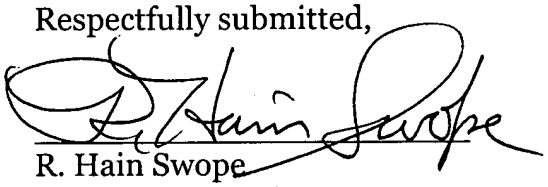
In regard to the determination of the total amount of BChE in the sample of biological fluid, Applicants note that the Examiner would appear to prefer "detecting". Applicants respectfully point out that they consider "detecting" to be a term of qualitative measurement and that determining is the preferable term for the quantitative measurement of the total BChE in the sample. In regard to the measurement of the total and unbound BChE in the sample by enzymatic or monoclonal antibody binding, Applicants do not consider that the claims should be limited to such methods, although preferred, because there are other art-recognized methods for carrying out the determination and it is the results of the determination, not the means of carrying it out that are essential to the claimed diagnostic method. Further, it is respectfully submitted that Claims 30-36, limited to the determination of BChE unbound to Con A vs. total BChE in the sample, are fully supported by Applicants' specification as filed.

Claims 35 and 36, equivalent to cancelled Claims 28 and 29, contain additional steps that have the effect of confirming the results of the determination of steps (1) through (4) of Claim 30. These claims, which are not extensively discussed in the Office Action under reply, provide an extra added measure of assurance to the screening diagnosis afforded by the steps recited in Claim 30. It is respectfully submitted that they meet the requirements of paragraphs one and two of 35 U.S.C. §112.

Accordingly, as Claims 3- through 36 meet the requirements of paragraphs one and two of 35 U.S.C. §112, it is respectfully submitted that the above-identified patent application is in condition for allowance. An early Notice of Allowance is respectfully solicited.

A Petition for a three month Extension of Time with the requisite fee is submitted herewith thereby providing for the timely filing of this Amendment.

Respectfully submitted,



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